

Economic analysis and health impacts of routine vaccination with TAK-003 dengue vaccine in San Juan, Puerto Rico

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Conflicts of interest & Disclosures

- GE and AP have previously received research funding from GlaxoSmithKline to support unrelated research on dengue vaccine development.
- AP currently receives research funding and consulting fees from Emergent Biosciences to support unrelated research on chikungunya vaccine development.
- As of June 2023, GE is an employee of CDC. This work was performed while working at the University of Notre Dame. The findings and conclusions in this presentation are those of the author(s) and do not necessarily represent the views of the CDC.

Terminology

Abbreviation	Full term/Meaning
VCD	Virologically confirmed disease
VE	Vaccine efficacy
DENV (e.g., DENV-3)	Dengue virus (e.g., serotype 3 dengue virus)
HPV	Human papillomavirus
PICO	Policy question articulated as P opulation, I ntervention, C omparison, O utcomes
Additional hospitalizations	Hospitalization induced by vaccine-enhanced disease
ICER	Incremental cost-effectiveness ratio (\$/QALY, \$/hospitalization averted)
QALY	Quality adjusted life years

We modeled six scenarios to answer each of the policy (PICO) questions.

- Age group scenarios:
 - 4 – 16 years
 - 17 – 60 years
 - 4 – 60 years
- For each age group we modeled:
 - Without required pre-vaccination screening (vaccinate seropositives and seronegatives)
 - With required pre-vaccination screening (vaccinate seropositives only)

Outcomes of interest included benefits, harms, and costs.

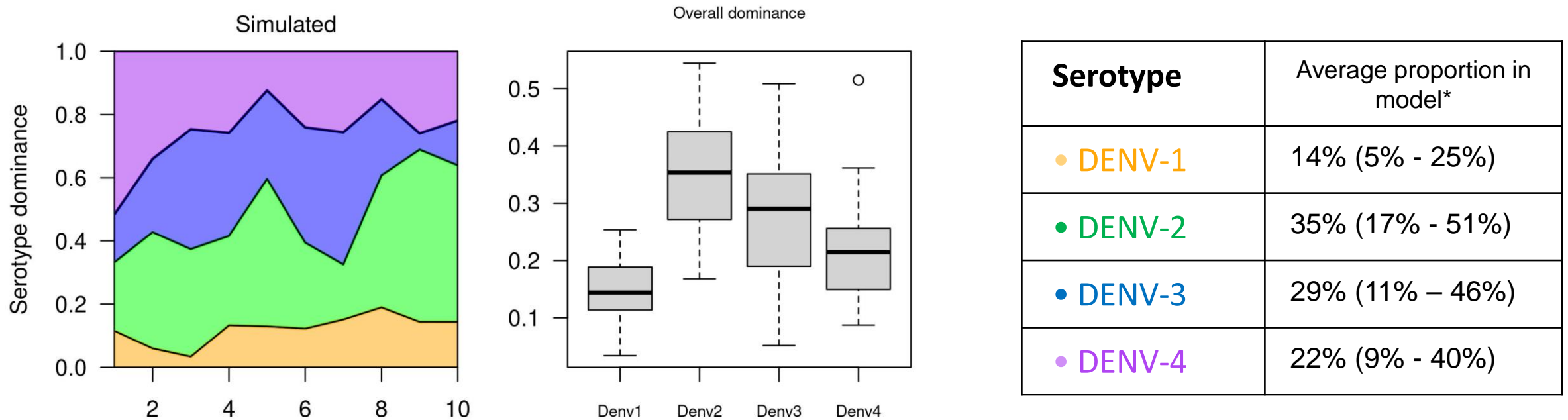
- Epidemiological outcomes:
 - VCD* and hospitalizations averted
 - Dengue hospitalizations among vaccinated seronegative persons infected with DENV-3 and DENV-4.
- Health Outcomes:
 - QALYs gained
- Economic outcomes:
 - ICER (\$/QALY)
 - ICER (\$/hospitalization averted)

*VCD refers to medically attended cases only

We calibrated an agent-based model to reproduce patterns of serotype circulation, force of infection, and age-specific incidence.

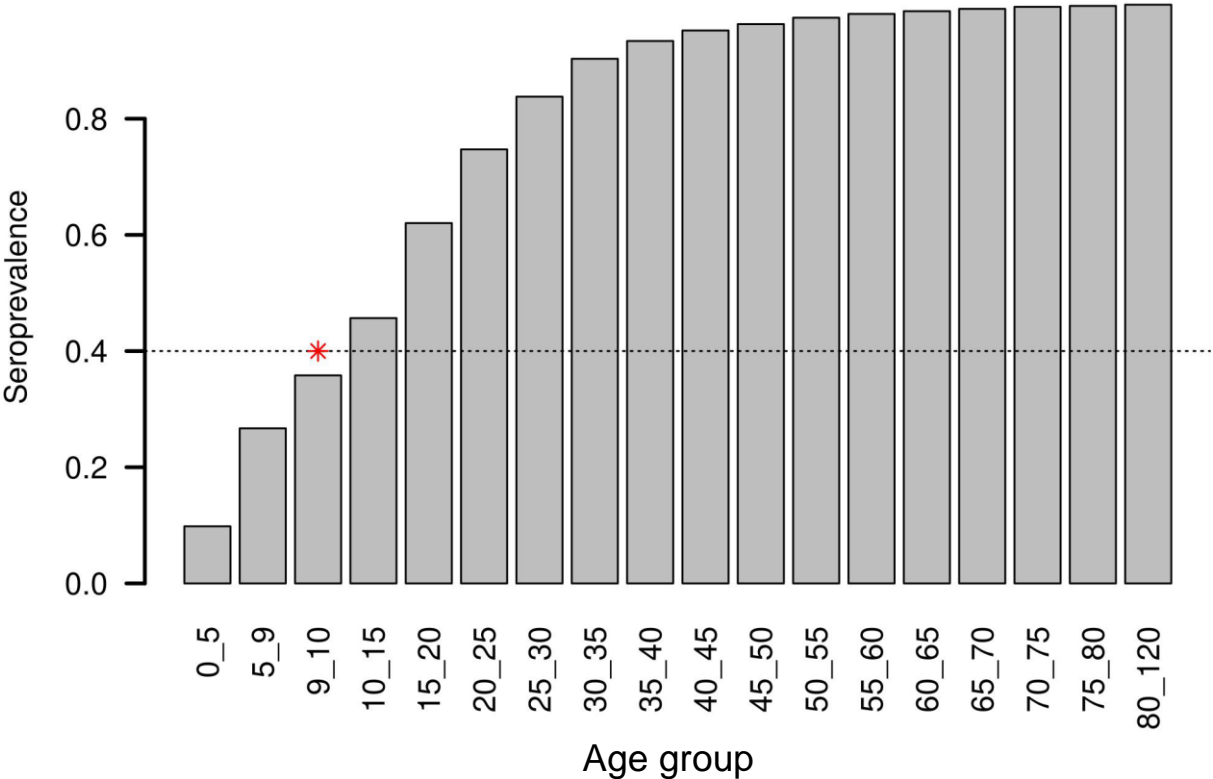
- We created a synthetic population to represent demographic and geographic characteristics of San Juan, Puerto Rico.
- Our model simulates individual daily activities of humans and mosquitoes.
- Model calibrated using 30 years of historical dengue surveillance data to reproduce observed force of infection and age-specific incidence.

The serotype distribution simulated over 10 year time horizon of vaccination was modeled on 30 (1986-2016) years of data from San Juan, Puerto Rico.



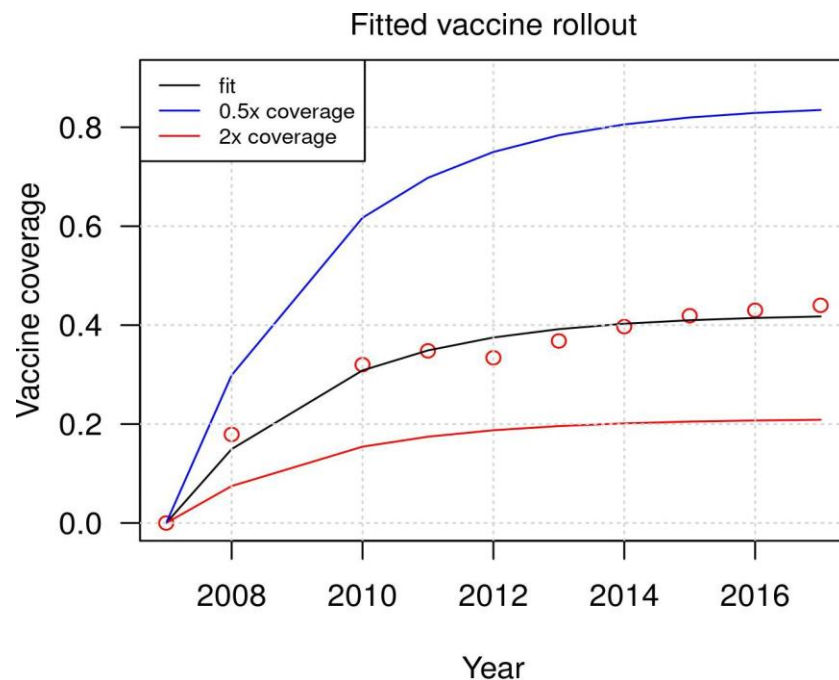
*Model based on 1,000 bootstraps with different proportion of serotypes in every simulation. Average reflects the mean proportion of serotypes among entire model. These estimates are preliminary and are subject to change.

The estimated seroprevalence among persons 9 years of age was approximately 40%.



- 30% of individuals aged 5–9 years were seropositive.
- People aged 20, 75% of people had ≥ 1 infection by the end of the calibration.

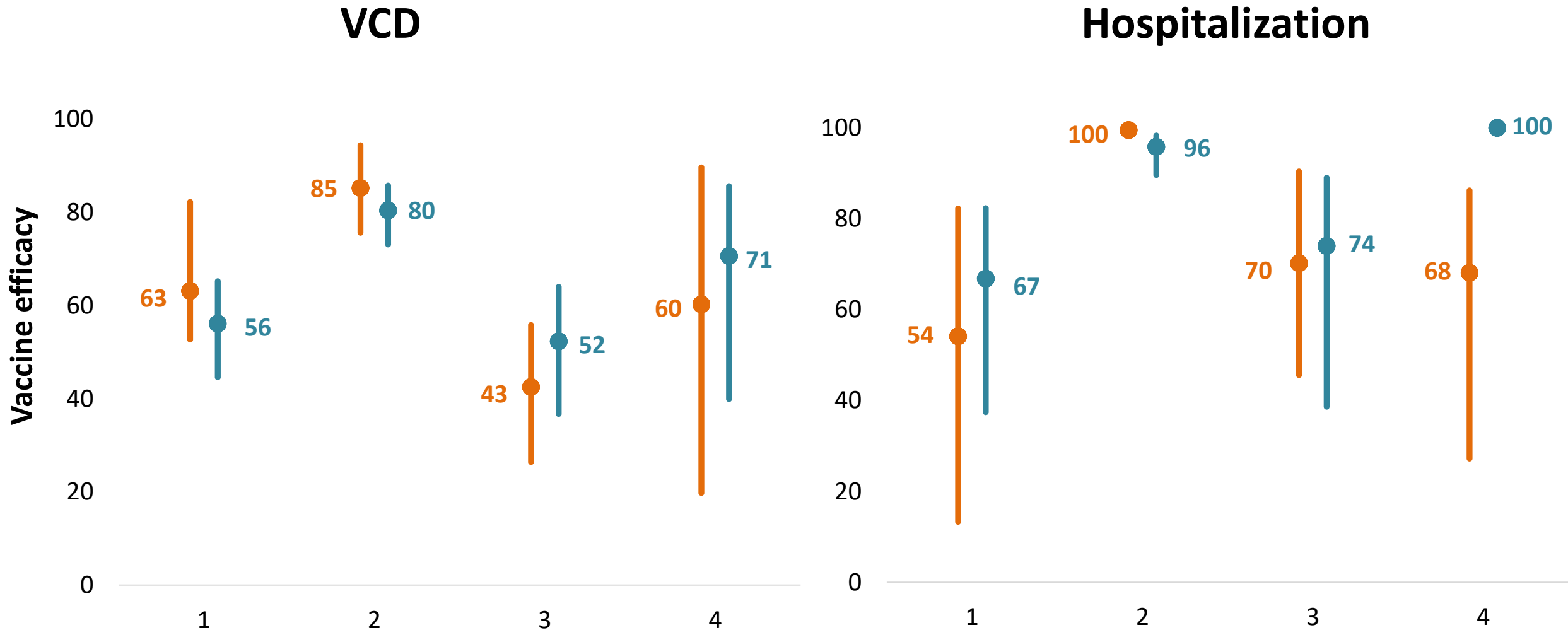
We simulated the vaccine roll-out based on previous introduction of HPV vaccine in the US*.



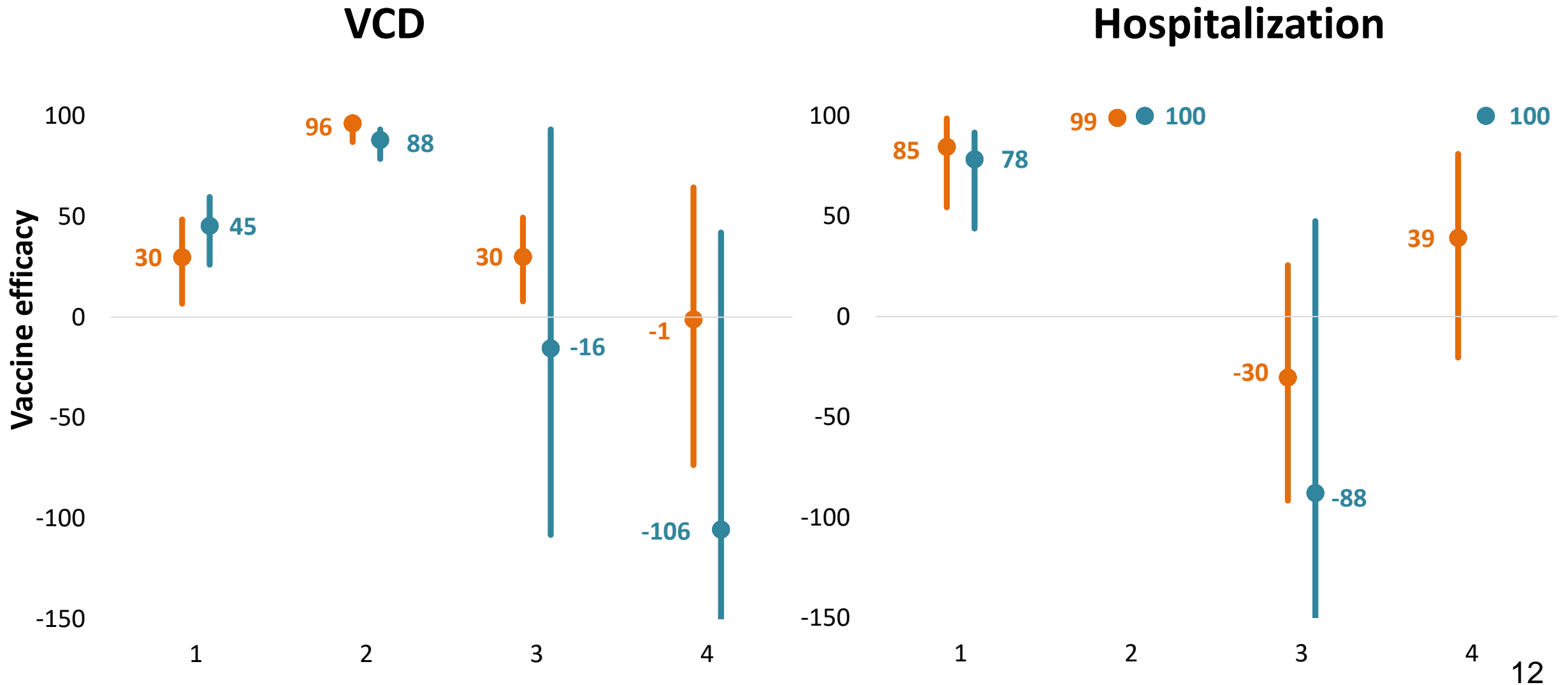
- Vaccine coverage increased gradually from 0% to ~40% in 10 years and was distributed evenly across age ranges in the scenario.
- We simulated additional scenarios of 2x and 0.5x the final coverage.

Vaccine efficacy and vaccine protection assumptions

Model and trial estimates of vaccine efficacy for VCD and hospitalization among seropositive participants.



Model and trial estimates of vaccine efficacy for VCD and hospitalization among seronegative participants.

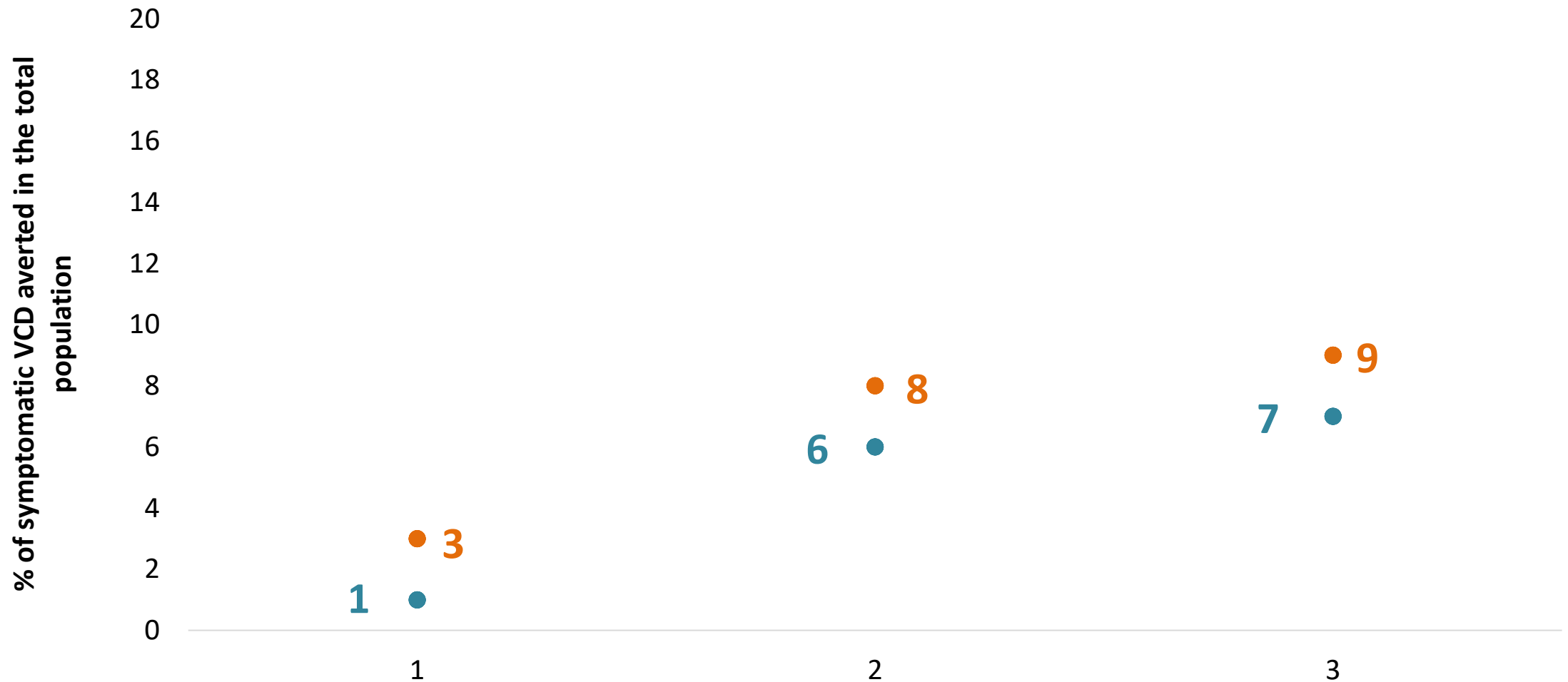


Vaccine protection assumptions

- Protection varies for each serotype (DENV 1-4) and serostatus (seronegative or seropositive).
- The duration of protection was estimated as
 - VCD for seronegatives (13.1yrs) and for seropositives (17.4yrs)
 - Hospitalization for seronegatives (19.3) and for seropositives (25.6).
- Equal level of protection against infection and disease given infection.
- In scenarios with pre-vaccination screening, the coverage of pre-vaccination screening is the same as the vaccine rollout coverage (without screening). The test has 80% sensitivity and 98% specificity for detecting previous dengue infection.
- We simulated outcomes of VCD and hospitalizations over 10 years in scenarios with vaccination compared to scenarios without vaccination.
- We assumed that all individuals testing positive are vaccinated.

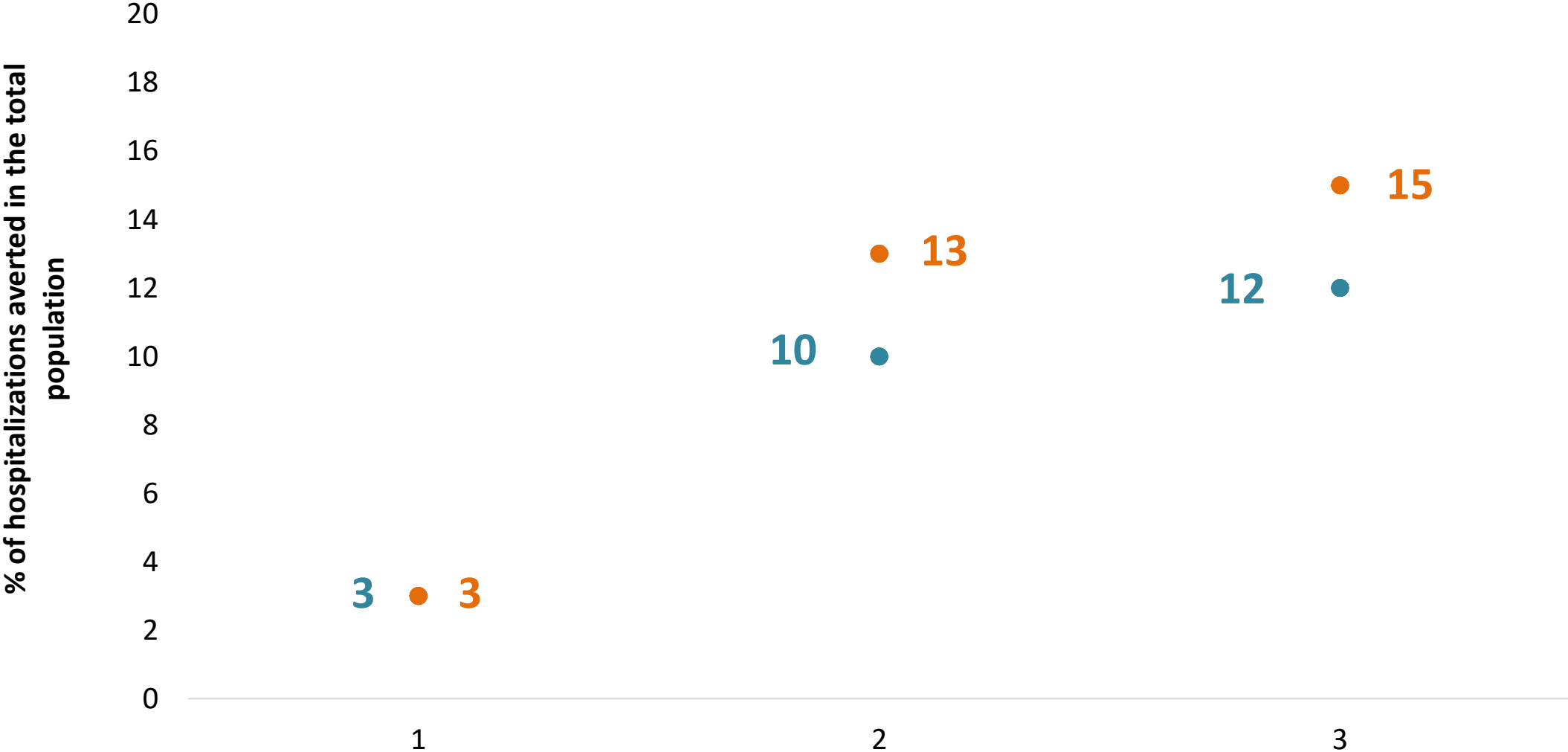
Epidemiological outcomes*: VCD and hospitalizations averted (Benefits)

No pre-vaccination screening increased the proportion of total VCD averted compared to screening.



*Results are preliminary and are subject to change.

No pre-vaccination screening increased the proportion of total hospitalizations averted compared to screening.



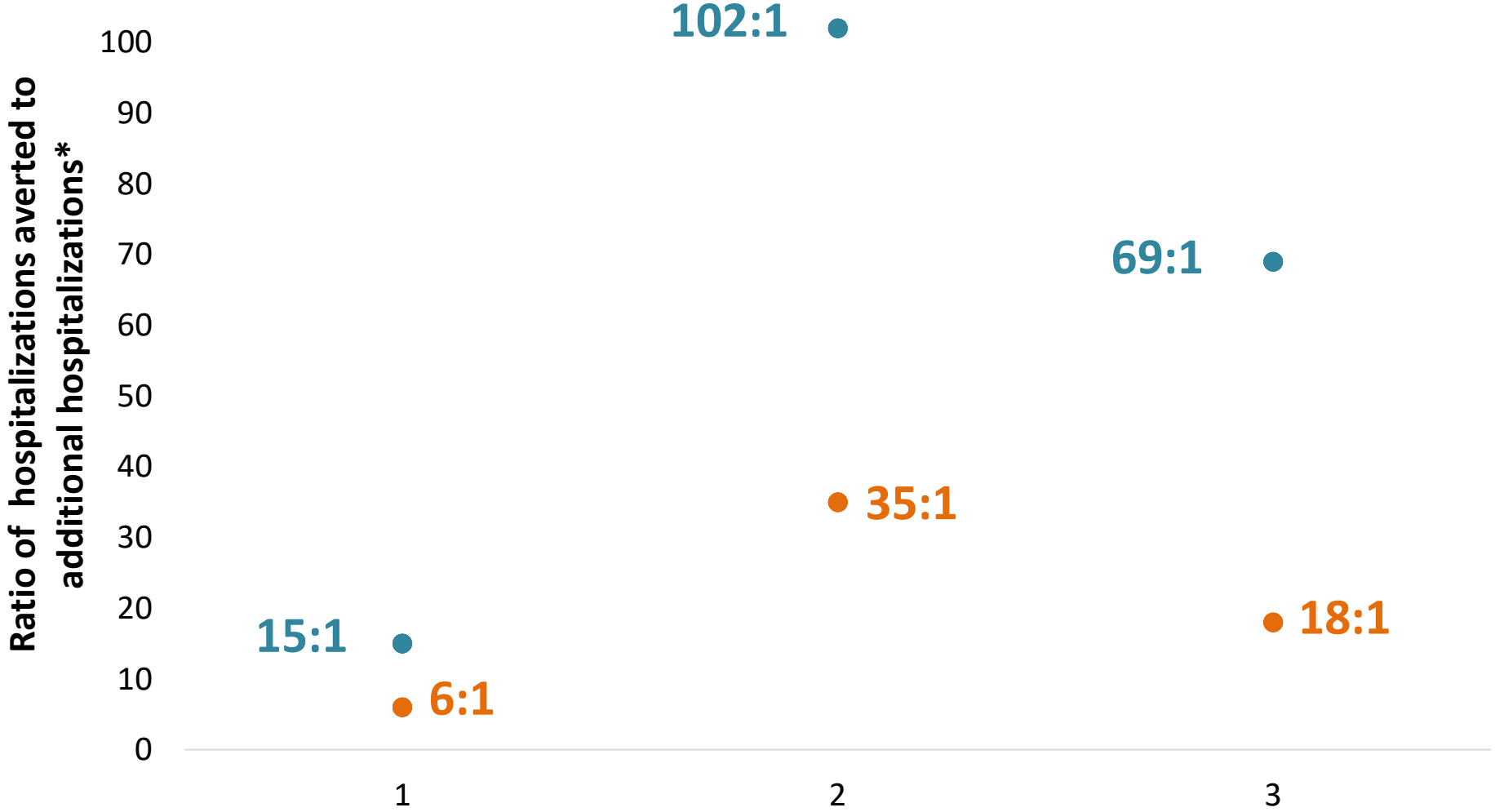
*Results are preliminary and are subject to change.

Epidemiological outcomes: Additional hospitalizations (Harms)

Outcomes: Additional hospitalizations (Harms)

- We used the ratio of averted hospitalizations to additional hospitalizations as a relative measure of harm.
- Additional hospitalizations only occurred among seronegative persons who received the vaccine and were infected with DENV-3 or DENV-4 post-vaccination.

Screening increased the ratio of averted to additional hospitalizations compared to no pre-vaccination screening.



*among seronegative persons who received the vaccine and were infected with DENV-3 post-vaccination. Note: Results are preliminary and are subject to change.

Economic outcomes*

We estimated the Incremental Cost-Effectiveness Ratio to determine cost-effectiveness

$$\frac{Cost_{intervention} - Cost_{no\ intervention}}{QALY_{intervention} - QALY_{no\ intervention}} = ICER$$

- We estimated the quality-adjusted life-years (QALYs) gained with routine vaccination using disability weights (Zeng et al. 2018)
- The unit cost per fully vaccinated individual was varied from 100 to 600 USD (330 USD baseline).

*The cost per fully vaccinated individual was estimated as 150 USD per dose with an additional 15 USD for vaccine administration costs per dose. All costs were estimated for the year 2022.

Economic outcomes* by scenario for a public payer perspective, over 10 years, 3% discounting.

Age group	Pre-vaccination screening	QALYs gained	ICER \$ / QALY gained	ICER \$ / hospitalization averted
4-16	Yes	17	181,918	16,800
4-16	No	35	254,751	46,813
17-60	Yes	89	396,574	48,986
17-60	No	118	314,597	39,886
4-60	Yes	106	384,830	48,305
4-60	No	134	326,412	45,495

*Results are preliminary and are subject to change.

Summary

- Our model simulations show some benefits from vaccination in terms of symptomatic cases and hospitalizations averted.
- These benefits depend on the serostatus of the vaccinees and the circulating serotypes.
- Overall, pre-vaccination screening reduces the potential negative outcomes in seronegative individuals.
- ICERs per QALY gained and ICER per hospitalization averted were higher when implementing pre-vaccination screening except in the 4–16 age group where screening was more cost-effective.
 - Cost-effectiveness of the intervention depended on the seroprevalence, which is lower for younger age groups.

Limitations

- Our model projections are not predictions on the serotype circulation or the burden of disease.
- Our results on the benefits and cost-effectiveness of the intervention depend on the circulation of specific serotypes during the projection period.
- We are not including QALYs loss due to death in the cost-effectiveness analysis.

Acknowledgements

This analysis is based on previous analyses described in the manuscript by España et al.: “Model-based assessment of public health impact and cost-effectiveness of dengue vaccination following screening for prior exposure. PLOS NTDs 2019” (España et al., [2019](#)). The manuscript was prepared in collaboration with other authors: Yutong Yao, Kathryn B. Anderson, Meagan C. Fitzpatrick, David L. Smith, Amy C. Morrison, Annelies Wilder-Smith, and Thomas W. Scott.

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